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Palladium diaqua and hydroxo complexes with polymer-supported BINAP ligands and their use for catalytic enantioselective reactions

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Abstract

We report the preparation of palladium complexes with the polymer-supported BINAP ligands, [Pd(PS-(*R*)-binap)$(H_2O)_2]^{2+}(BF_4^-)_2$ (**5**) and [{Pd(PS-(*R*)-binap)(μ-OH)}$_2]^{2+}(BF_4^-)_2$ (**9**). These complexes were shown to be good catalysts for asymmetric aldol reactions and Mannich-type reactions, and also to be reusable. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: palladium; solid-supported catalysts; enantioselection; aldol reactions; Mannich reactions.

The use of asymmetric carbon–carbon bond forming reactions catalyzed by chiral transition metal complexes is now becoming an important technology for organic synthesis. Unlike asymmetric hydrogenation reactions, in which a large excess of one reagent, hydrogen, can be used, the catalytic turnover of carbon–carbon bond forming reactions is not usually high. One approach to solving this problem is catalyst recycling. The development of polymer-immobilized asymmetric catalysts is a topic of growing interest.[1,2] Since recent progress in solid-phase synthesis technology including the development of various automated machines has been outstanding, it would not be difficult to build an automated recycling reaction system, if we had good, reusable, polymer-supported catalysts. Immobilization of catalysts, however, often results in catalysts with lower enantioselectivities or efficiencies than their solution phase counterparts. We have reported an asymmetric aldol reaction[3] catalyzed by a palladium BINAP diaqua complex **1** and a Mannich-type reaction[4] catalyzed by a palladium BINAP μ-hydroxo complex **2** (Fig. 1).

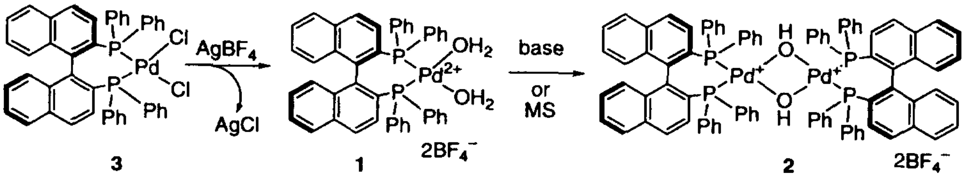

Figure 1.

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We planned to develop polymer-supported catalysts for these unique reactions in which the reactions proceeded via a chiral palladium enolate. Here we report the preparation of novel polymer-supported BINAP palladium diaqua and hydroxo complexes, and their use as efficient asymmetric catalysts.

We prepared the catalyst **1** by the reaction of the palladium dichloride complex **3** with silver tetrafluoroborate.[3b] In applying this method to the polymer-supported complex, however, we had trouble separating the byproduct, insoluble silver chloride. Since optically active polystyrene-supported BINAP **4** (PS–BINAP) has recently become commercially available,[5] we examined several possibilities for using it. As a result, we were pleased to find that treatment of (*R*)-**4** (0.45 mmol/g) with $[Pd(CH_3CN)_4]^{2+}(BF_4^-)_2$ (1 equiv.) in wet acetone (H_2O 0.5% v/v) under an argon atmosphere at room temperature for 6 h gave the desired polymer-supported aqua complex (*R*)-**5** as a dark red resin (calculated Pd load: 0.38 mmol/g) (Fig. 2). Comparison of the IR spectrum of this resin to that of (*R*)-**4** clearly indicated that this resin was the desired dicationic aqua complex, (*R*)-**5**.[6,7] It showed a very strong band at 1090 cm^{-1} which can be assigned as the ionic BF_4^-.[8] The presence of coordinated water molecules was confirmed by the strong O–H stretching absorption at 3450 cm^{-1} and the small H–O–H bending band at 1630 cm^{-1}. Similar bands were also observed in the spectrum of (*R*)-**1**.

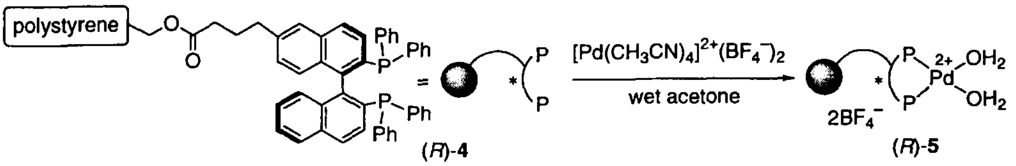
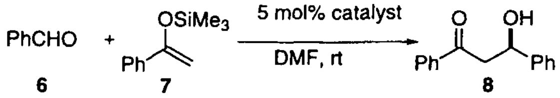


Figure 2.

Table 1
Asymmetric aldol reaction using aqua Pd complexes **1** and **5**



entry[a]	catalyst	H_2O (equiv)	time (h)	yield (%)	ee (%)
1	(*R*)-1	–	17	65	74
2	(*R*)-5	–	35	35	76
3	(*R*)-5	0.2	20	94	74
4	(*R*)-5[b]	0.2	40	81	71

[a] A solution of the catalyst (5 mol %), **6**, and **7** (1.5 equiv) in dry or wet DMF was stirred at room temperature for the indicated time. The product **8** was isolated after acid treatment. The ee was determind by HPLC analysis using DAICEL Chiralcel OJ.[3a]

[b] Recovered catalyst from the reaction of entry 3 was used.

Results of the reaction of benzaldehyde (**6**) with the enol silyl ether **7** using this novel resin catalyst are shown in Table 1. Reaction in dry DMF using (*R*)-**5** (5 mol%) as a catalyst afforded the aldol **8** of comparable ee (76% ee) to that of the product from the reaction using the soluble catalyst **1** (entries 1 and 2). The chemical yield, however, was only 35%. As observed in the reaction using a catalyst prepared from $[PdCl_2((R)\text{-binap})]$ and $AgBF_4$ in situ,[3a] addition of a small amount of water accelerated the reaction, and the chemical yield improved to 94%. The enantiomeric excess of the product was the same as that of entry 1 using (*R*)-**1** (74% ee) (entry 3). As reported before,[3b] crystals of **1** usually contain two waters of crystallization per Pd in addition to the two coordinated waters, and the extra waters enhance the reaction. The water effects observed in the reaction using (*R*)-**5** suggest that (*R*)-**5** would not have such extra water of crystallization. Next we tried recycling the used catalyst. After the first reaction, the catalyst was easily separated from the reaction mixture by simple filtration. This resin was

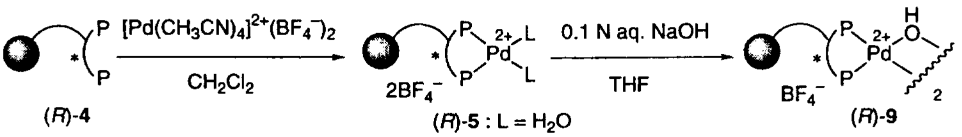
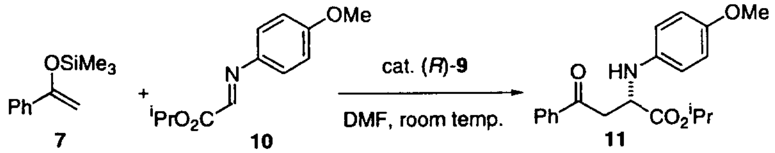


Figure 3.



95%, 81% ee
72%, 71% ee (2nd)

Figure 4.

washed with THF and then wet acetone and dried under vacuum. The same reaction was carried out using this recovered catalyst to give **8** in 81% yield. The ee of the product is almost as good (71% ee). The treatment of the resin with wet acetone is important to maintain reactivity. Excessive washing with dry solvent would remove the coordinated water from the complex and retard the reaction, although the ee of the product would be unchanged.[9]

As we reported before,[4] the reaction of **7** with imines, the so called asymmetric Mannich-type reaction, using aqua Pd complexes such as **1** was unsuccessful. The use of less-acidic binuclear μ-hydroxo Pd complex such as **2** was critical for high asymmetric induction. Thus, next we planned to prepare a polymer-supported hydroxo Pd complex. The free ligand (*R*)-**4** was first treated with $[Pd(CH_3CN)_4]^{2+}(BF_4^-)_2$ (1 equiv.) in CH_2Cl_2 under an argon atmosphere at room temperature for 6 h (Fig. 3).[10] After washing (dry CH_2Cl_2) and drying under vacuum, the resin was then treated with a mixture of 0.1N aqueous NaOH solution (1 equiv.) and THF at room temperature for 3 h.[11] After washing with THF–H_2O and then dry THF, and drying under vacuum, (*R*)-**9** was obtained.[12] The IR spectrum of (*R*)-**9** showed a sharp band at 3580 cm^{-1} which is characteristic of the O–H stretching absorption of the hydroxo-bridged binuclear Pd complexes.[13,14] Strong absorption at 1065 cm^{-1} indicated the presence of BF_4^-.[8]

Using this resin as a catalyst (20 mol% Pd calculated as 0.41 mmol/g) the reaction of imine **10** with enol silyl ether **7** (2 equiv.) at room temperature in DMF was carried out (Fig. 4). The desired benzoylalanine derivative **11** was obtained in 95% chemical yield and 81% ee. Thus, (*R*)-**9** proved to be a good catalyst for the asymmetric Mannich-type reaction, although the ee was slightly lower compared to the reaction using **2** (89% ee).[4] After the reaction, the resin was separated from the reaction mixture by filtration and washed with dry THF. The active catalyst was regenerated by a base treatment which was similar to the procedure for the preparation of (*R*)-**9** from the dicationic complex. The reaction using this resin also proceeded smoothly to give **11** in 72% yield. The ee of the product was 71%. The base treatment is essential for the regeneration of the active catalyst to give high ee. Reuse of the resin without this base treatment caused a drastic decrease of the ee to 25%. Although further optimization of the conditions for regeneration of the catalyst remains to be done, the resin was shown to be reusable with reasonable efficiency.

In summary, we have synthesized palladium complexes with the polymer-supported BINAP ligand, $[Pd(PS\text{-}(R)\text{-}binap)(H_2O)_2]^{2+}(BF_4^-)_2$ (**5**) and $[\{Pd(PS\text{-}(R)\text{-}binap)(\mu\text{-}OH)\}_2]^{2+}(BF_4^-)_2$ (**9**). The aqua complex (*R*)-**5** and the μ-hydroxo complex (*R*)-**9** were found to be good catalysts for the asymmetric aldol and Mannich-type reactions, respectively. These catalysts were reusable after an appropriate refreshing treatment.

Acknowledgements

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5. Purchased from Oxford Asymmetry International. Although the ligand described in the literature[2e] has an amide linkage, the commercially available one has an ester linkage. See: Bayston, D. J.; Fraser, J. L.; Ashton, M. R.; Baxter, A. D.; Polywka, M. E. C.; Moses, E. *Speciality Chemicals* **1998**, *18*, 224–226.
6. IR (KBr): (*R*)-**4**: 3030, 2925, 1740, 1600, 1495, 1455, 750, 700, 540 cm^{-1}; (*R*)-**5**: 3450, 3030, 2930, 1740, 1630, 1605, 1495, 1455, 1090, 750, 700, 540, 522, 505 cm^{-1}; (*R*)-**1**: 3440, 3060, 1625, 1440, 1085, 750, 700, 522, 505 cm^{-1}.
7. Gel phase ^{31}P NMR analysis (in $CDCl_3$, H_3PO_4 as an external standard) of the series of resins was carried out. The free polymer-supported ligand (*R*)-**4** showed a peak at −15.28 ppm. It is in good agreement with that of free BINAP (−15.33 ppm). The aqua complex (*R*)-**5** showed a broad peak at 31.43 ppm, whereas that of (*R*)-**1** was 34.02 ppm. For an example of monitoring solid phase reactions by ^{31}P NMR, see: (a) Johnson, C. R.; Zhang, B. *Tetrahedron Lett.* **1995**, *36*, 9253–9256. (b) Uozumi, Y.; Danjo, H.; Hayashi, T. *Tetrahedron Lett.* **1997**, *38*, 3557–3560.
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9. Analysis of the reaction mixture for Pd content by ICP-AES (inductively coupled plasma atomic emmision spectroscopy) showed that less than 3 mol% of the total amount of Pd used was leached into the solution phases (for Aldol reaction: 2.8 mol%; for Mannich-type reaction: 1.7 mol%).
10. Although dry CH_2Cl_2 was used for this reaction, the IR spectrum of the resin showed (*R*)-**5** with waters as ligands was also formed by this procedure. A small amount of water absorbed from the air during the workup and/or IR measurement may be sufficient to form the aqua complex.
11. Our original procedure for the preparation of (*R*)-**2** using aq. NaOH–CH_2Cl_2 was not effective for preparation of (*R*)-**9** because the three phase separation (water, CH_2Cl_2, and solid phases) would make the reaction ineffective. The resin prepared by the base treatment of the aqua complex (*R*)-**5** using CH_2Cl_2 instead of THF gave lower asymmetric induction.
12. Although a sharp peak at 29.22 ppm was observed in the ^{31}P NMR spectrum of (*R*)-**2**, it was difficult to detect a peak in the spectrum of (*R*)-**9**. Only a quite broad peak at 25–35 ppm was observed. Usually the more the movement of a phosphorous atom is restricted, the more broadening of the ^{31}P NMR spectrum would be observed. It is reasonable that the binuclear μ-hydroxo Pd complex on the polystyrene resin is more rigid compared to that of the corresponding aqua complex resin, and shows a quite broad peak.
13. IR (KBr): (*R*)-**9**: 3590, 3030, 2925, 1735, 1600, 1495, 1455, 1065, 910, 750, 700, 540, 520, 500 cm^{-1}; (*R*)-**2**: 3590, 3060, 1630, 1440, 1090, 1060, 750, 700, 530, 500 cm^{-1}.
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